on the ballots in the primary election? Do you know aught concerning their general reactions to public health legislation? Officers of Component county societies and their committees on public policy and legislation have here a very special responsibility!

May the hope be expressed that every physician who is in position to contact incumbent and prospective legislators will do his part for organized and scientific medicine and the public health? A let-down in medical practice standards could pave the way for less efficient care of our soldiers who are in the armed forces. Attention by physicians to their civic responsibilities, therefore, becomes a patriotic as well as a professional obligation. Let us not be found wanting.

NEXT ANNUAL SESSION

When Program-Making Begins.—Program and other plans for a succeeding year's annual session take on beginning form almost immediately after the concluding day of the convention of a current year. For the annual gathering to be held next year at Hotel Del Monte, the Council of the Association has authorized the Committee on Scientific Work to arrange programs somewhat in accord with the plan carried through for the 71st Annual Session, recently held. Should unforseen complications arise in the meantime, the tentative arrangements will be changed.

The return to a larger number of general meetings has met with general approval. In May last, the general meetings were held on Monday, Tuesday and Wednesday mornings, and on Tuesday afternoon, and the attendance on each day was excellent. Members were able to outline their schedules in manner to permit visits at convenient times to scientific and technical exhibits and medical and surgical film presentations. The twelve scientific sections in the specialties accordingly arranged their work for Monday and Wednesday afternoons, the larger sections also presenting programs on Tuesday afternoon.

The value of the Sunday meetings has been referred to in previous issues, and will be increasingly evident during the duration, since conservation of the time of physicians cannot be disregarded. Members who have never attended meetings of the Sunday groups and activities may well refer to the "Program: By Days" in the April issue of the OFFICIAL JOURNAL (pages 177 and 195-196) and note how well the time may be spent. For those who prefer utter rest and relaxation, the Del Monte and Monterey Peninsula environment offer many facilities.

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Next Year's Essayists Should Communicate with the Proper Section Officers.—The names of officers of the twelve Scientific Sections appear in every issue of CALIFORNIA AND WESTERN MEDICINE on adv. page 6. Every member who contemplates possible presentation of a paper at next year's annual session should refer to this list, and at an early day write to the proper Section Secretary in regard to the prospective paper. Section officers and the C. M. A. Committee on Scientific Work will appreciate such coöperation. Concerning scientific exhibits and medical and surgical films, correspondence should be sent to the Association Secretary, who is in charge of these activities.

The joint meeting of the C. M. A. Committee on Scientific Work and the Section Secretaries will be held early in the Fall. It will make for the presentation of high-standard programs in 1943, if members of the Association who are in position to take part in the meetings, will communicate in the meantime with the proper officers.

CALIFORNIA AND WESTERN MEDICINE: PRINTING OFFICE

Why Printing Office Was Changed.—After investigation last year, the Council learned that a considerable money-saving in printing expense of the CALIFORNIA AND WESTERN MEDICINE could be made, if the OFFICIAL JOURNAL would be brought off the press in Los Angeles. Accordingly in January last, the change in printing office was made. Under the new arrangement, the June issue will complete Volume 56.

The task of transfer concerning printing arrangements has not been easy, but the hope is expressed that readers will feel that CALIFORNIA AND WESTERN MEDICINE is again taking on its former typographical appearance and format. The new printers have been fully coöperative.

Owing to the late date on which the transcription of the minutes of the House of Delegates was received, it is not possible to have them appear in the June number.

EDITORIAL COMMENT†

"MASKED CARCINOGENIC VIRUS

It is currently reported by Kidd[1] of the Rockefeller Institute that "masked" V_2 papilloma virus is able to multiply in the bodies of virus-immune rabbits, a seeming paradox with suggestive bearings on the therapy of numerous other virus diseases.

About ten years ago it was shown by Shope[2] that the horny cutaneous growths, common to the wild cottontail rabbits of the Middle West, are due to a filterable virus. The disease is readily transferred to domestic rabbits by rubbing papilloma extract (or filtrate) into slightly scarified

† This department of CALIFORNIA AND WESTERN MEDICINE presents editorial comments by contributing members on items of medical progress, science and practice, and on topics from recent medical books or journals. An invitation is extended to all members of the California Medical Association to submit brief editorial discussions suitable for publication in this department. No presentation should be over five hundred words in length.

(sand papered) skin. In both wild and domestic rabbits, the resulting local papillomas tend to become malignant, giving rise to invasive subcutaneous growths, with metastases in regional lymph glands, lungs and other internal organs. While the resulting malignant growths[3] are readily transplantable into normal rabbits, the papilloma virus has never been recovered from them. Extracts and filtrates from metastatic nodules are wholly noninfectious when rubbed into slightly scarified normal rabbit skin.

Shope found that the serums of rabbits, either naturally or experimentally infected with the papilloma virus, contain antibodies that completely neutralize the virus in vitro, and that rabbits with high titer antiserums are practically immune to experimental percutaneous inoculation of the virus containing filtrate. It was afterwards demonstrated by Kidd and Rous[4] that the apparently virus-free secondary metastatic nodules are also capable of stimulating specific antibody production in normal rabbits. Antibodies, capable of neutralizing the Shope papilloma virus, appear in the blood of every new host in which the carcinoma enlarges progressively. A detailed study of the specificity of these antibodies led to the conclusion that the carcinoma cells must contain some relatively inactive phase of the original papilloma virus. Such a "masked"[5] virus is presumably incapable of infecting normal rabbit skin, but is apparently still capable of stimulating specific antibody production. This hypothetical "masked" papilloma virus is currently referred to as the "V_2 carcinoma virus."

The conclusion, that "masked" papilloma virus is the essential etiologic factor in the secondary carcinomas, renders the relationship of the "masked" virus to the primary anti-viral antibodies of basic clinical interest. In order to test this relationship, Kidd attempted to propagate the metastatic carcinoma in the bodies of virus-immune rabbits.

To prepare animals for this test a potent papilloma filtrate was rubbed on the freshly-scarified skins of a number of rabbits, followed two to three weeks later by multiple intraperitoneal injections with the same filtrate. About ten days after the last injection, the rabbits were bled from an ear vein, and their virucidal titers determined. Serums thus obtained had a complement fixation titer of from 1:32 to 1:128 when tested with the filtrate, previous work showing that a serum of even 1:24 titer is capable of neutralizing many thousand infectious doses of virus, and that an animal yielding this titer is usually completely resistant to percutaneous infection with the virus.

Transplantations of the metastatic carcinoma were effected by preparing a fine suspension of malignant tissue cells in 10 per cent homologous immune serum (Tyrode's solution). One cc. portions of this suspension were implanted in six of the leg muscles of the virus-immune hosts, both forelegs and thigh muscles being used. The malignant growths used in preparing these cellular suspensions had already been propagated for 2 years (12 generations) in normal (nonimmune) domestic rabbits. Injected into six leg muscles of a control nonimmune domestic rabbit the suspension led to the appearance of 5 palpable nodules ranging from 1.2 to 3.2 cm. in diameter by the 42nd day. During the ensuing 8 weeks all five malignant growths enlarged rapidly, reaching 7.5 to 10 cm. in diameter by the 107th day.

Injected into six hyperimmune rabbits, progressively enlarging carcinomas developed in three animals, early regression was noted in one rabbit, with no palpable tumors in the other two. By the 40th day, the three positive growths had reached 3.5 to 7.4 cm. in diameter. From these tumors Tyrode-immune serum cell suspensions were made for transplantation into a second group of hyperimmune rabbits, and the process repeated for five hyperimmune generations. The fifth generation growth was then returned to a group of normal rabbits, in which it grew rapidly and stimulated the production of specific antiviral (antipapilloma) antibodies. From their statistical evidence there is no doubt that Shope carcinoma can be propagated as well in animals hyperimmune against the initial papilloma virus, as in normal controls, and that antiviral (antipapilloma) antibodies have no inhibiting effect on the rate of propagation of the accompanying "masked" virus.

It is of theoretical interest to speculate upon the mechanism whereby the living carcinoma cells protect the "masked" virus from neutralization by circulating antibodies. The simplest assumption would be that the virus lives within the cancer cells and is thus protected from contact with humoral antibodies. It is conceivable, however, that the antibodies might be ineffective even if they came into contact with the "masked" virus. Such might be the case if the virus underwent a transient chemical mutation, transformation or conjugation into a secondary carcinogenic phase. So altered its new antigenicity might render it resistant or insusceptible to the primary antiviral antibodies.

This would be analagous to the well-known antigenic mutations[6] of the spirochetes of relapsing fever.

From a practical viewpoint, however, demonstration of the proliferation of the "masked" virus, in spite of an adequate humoral immunity, has a suggestive bearing on current methods of specific diagnosis, prophylaxis and therapy of numerous other virus diseases, complexities largely overlooked in conventional clinical logic.

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CUTANEOUS HYPERINFECTIVITY

Methods of increasing the microbic susceptibility of normal skin a hundred-fold by previous treatment with certain chemical agents are currently reported by Friedewald[1] of the Rockefeller Institute. Applying this new technique he was able to detect and isolate the "masked" virus in certain malignant growths, which previous investigators[2] had found to be wholly noninfectious.

A Berkefeld filtrate of an aqueous extract of the naturally-occurring papillomas of cottontail rabbits contains a virus which, when rubbed into slightly scarified (sandpapered) skin of domestic rabbits produces papillomas whose size, number and time of appearance are in mathematical relationship to virulence and dosage. On a standard scale of severiy, the lesions vary from a few small discrete papillomas (+), through many slightly larger discrete warts (++), to semi-confluent papillomas (+++), and finally to large confluent masses 1.5 to 2 cm. in height (++++). By means of this standard severity scale, unknown samples of this virus can be accurately titrated.

Using this scale, Friedewald tested the changes in size and severity of the growths produced by standard doses of virus rubbed into adult rabbit-skin which had been previously treated with physical or chemical irritants. Among the irritants tested were single or multiple exposures to x-ray or ultra-violet light, single or multiple applications of tar or other carcinogenic agents, as well as repeated applications of a number of noncarcinogenic chemicals, such as equal parts of turpentine and acetone, or 0.3 per cent methylcholanthene in benzene.

He found that within the limits of the experimental error, acute inflammation produced by x-ray or ultra-violet light did not alter normal skin susceptibility. Something approaching a 10-fold increase in the size or number of the resulting lesions, however, was noted in skins previously treated with certain (but not all) carcinogenic agents. An approximate 100-fold increase in severity was noted as a result of previous treatment with turpentine-acetone, or with 0.3 per cent methylcholanthene in benzene. In one series of rabbits, for example, the minimum infectious dose for normal skin was a 1:100,000 dilution of the selected virus. A 1:10,000,000 dilution of the same virus proved infective for turpentined skin. The increased susceptibility was also shown by a marked shortening of the incubation period, and by a marked increase in the size and complexity of the resulting papillomatous growth. In one series, for example, large confluent masses 1.6 cm. or more in height were noted on the treated skins, as contrasted with a few discrete warts less than 0.4 cm. high on the normal skins, a ratio of 135:1 in the sizes of the new growths.

Tests showed that a single application of these virus-enhancing chemicals did not appreciably increase skin susceptibility. Skins treated three times at two-day intervals, however, became highly susceptible, with but slight further increases in susceptibility as a result of six applications. The increased skin sensitivity persists for about two weeks, with complete loss of the acquired hyperinfectivity by the end of four weeks.

As a practical application of the new technique the Rockefeller Institute pathologists found that they were able to demonstrate papilloma virus in extracts of domestic rabbit "V2 carcinomas," which previous investigators[3] had found to be noninfectious for normal domestic rabbit-skin. They were thus able to confirm the conclusion of the previous investigators that these carcinomas contain a "masked," "latent" or "cryptic" virus. This is a particularly significant finding, since it suggests a new method of experimental study of the possible virus etiology of human cancers and other controversial diseases.

Histological studies showed that the various agents which enhance virus susceptibility all cause the epidermis to proliferate actively, thus providing numerous young, actively-regenerating cells. These are presumably especially susceptible to bacterial and virus infections. Whether or not the same hyperplastic hypersusceptibility can be produced on mucous surfaces, however, has not yet been determined.

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Ludwig's Angina

Wilhelm Friedrich von Ludwig (1790-1865) communicated his vivid description of "a variety of inflammation of the neck which has recently been of frequent occurrence in this community" to the *Medicinisches Correspondenz-Blatt des Württembergischen Ärtzlichen Vereins* (6:21, 1836). A portion of the translation follows:

"After a series of prodromal symptoms . . . there develops a firm swelling . . . usually in the cellular tissue surrounding the submaxillary gland. This . . . swelling spreads around the neck under the jaw . . . with marked lateral bulging. . . . The tongue lies on a floor of . . . indurated bright-red tissue, which feels like a hard, calloused ring along the inner border of the jaw inside the mouth. . . . Ability to open the mouth is restricted and painful . . . speech is difficult . . . thick and gurgling. . . . The skin, . . . in the early stages at least, is very slightly reddened if at all and is normal in texture; . . . later, soft red spots may appear . . . but no pus is ever formed. . . . The symptoms of the subsequent rapid course are those of a putrid-typhoid process, and in four to five days, the tenth to twelfth from the onset of the illness, coma develops and death occurs with indications of respiratory paralysis."—R. W. B., in *New England Journal of Medicine.*